

WHAT IS CLAIMED IS:

1. A method for screening of the presence or absence of variation in a region of a nucleic acid comprising the steps of:

5 (a) preparing a test nucleic acid corresponding to the region;

(b) preparing a probe having a base sequence fully complementary to a normal sequence of the region, and a plurality of probes each having at least one base not complementary to the normal sequence;

10 (c) fixing the probes in separate regions on a surface of a substrate to prepare a DNA array substrate;

(d) reacting the test nucleic acid with the probes on the DNA array substrate;

15 (e) measuring signals in each region totally where the signals are originated from respective hybrids formed between the test nucleic acid and one of the probes; and

20 (f) determining the presence or absence of mutation in the test nucleic acid comparing with a histogram pattern of signals of all regions obtained using a normal sample without variation.

25 2. The method according to claim 1, wherein the signal is a light emitted from each hybrid and the total signal is measured as a total light quantity

emitted from each region.

3. The method according to claim 2, wherein the light is fluorescence.

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4. The method according to claim 2, wherein the light is a chemical luminescence.

10 5. The method according to claim 1, wherein the steps (c) to (e) are:

(c) preparing separated regions on a substrate by fixing probes on a surface of the substrate, wherein the separate regions comprises:

15 a first region containing probes which provide a signal of a certain intensity on reaction with a nucleic acid having normal sequence,

a second region containing probes which provide weaker signals on reaction with a nucleic acid having normal sequence, and

20 the third region containing probes which do not form hybrids on reaction with a nucleic acid having normal sequence;

25 (d) reacting the DNA array of step (c) with a nucleic acid having normal sequence and measuring a signal of at least one region selected from the three regions to obtain a first pattern; and

reacting the DNA array of step (c) with the test

nucleic acid, and measuring a signals of at least one region corresponding to the selected region of the step (d) to obtain a second pattern; and

(e) determining the presence or absence of variation in the test nucleic acid by comparing the first and second patterns.

6. The method according to claim 5, wherein the selected region is the first region giving a strongest total signal and/or the third region giving no or a weakest signal on reaction with a nucleic acid having normal sequence.

7. The method according to claim 5, wherein the  
15 separate regions are arranged on the substrate in order  
of signal intensity obtainable by reacting with a  
nucleic acid having normal sequence, from the highest  
intensity to the lowest intensity along a direction of  
a detection.

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8. The method according to claim 5, wherein the selected region is the third region, and when a total signal is detected with the test nucleic acid in the step (d), variation is called positive, and the test nucleic acid is determined to have variation.

9. The method according to claim 5, wherein the

first region contains probes consisting of a probe  
having a fully complementary sequence to the normal  
sequence and probes having one-base mismatch to the  
normal sequence. When reacting with a normal base  
sequence of a nucleic acid.

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10. The method according to claim 5, wherein the  
selected regions are both of the first and the third  
region and determining the presence or absence of  
variation comparing the ratio of the intensity of the  
10 region to that of the first region.

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11. The method according to claim 5, wherein the  
selected regions are all of the region, and determined  
the presence of absence of variation comparing the  
histogram pattern of signal intensity.

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12. The method according to claim 5, wherein  
detection of the total signal is performed by an area  
20 sensor.

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13. The method according to claim 7, wherein  
detection of the total signal is performed by a line  
sensor.

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14. The method according to claim 1, wherein a  
base length of the probes is 8 mer to 30 mer.

15. The method according to claim 14, wherein the base length of the probes is 12 mer to 25 mer.

16. A DNA array substrate for screening a variation in a region of a nucleic acid, wherein 5 a full match probe fully complementary to a normal sequence of the region, and a plurality of mismatch probes having at least one base mismatch to the sequence are arranged on the substrate; and

10 the probes are arranged to form at least two separate regions selected from:

a first region containing at least one probe which provides a signal of a certain intensity on reaction with a nucleic acid having the normal sequence,

15 a second region containing at least one probe which provides a weaker signal than the probe of the first region on reaction with a nucleic acid having normal sequence, and

20 the third region containing at least one probe which provides no signal on reaction with a nucleic acid having normal sequence.

17. The DNA array substrate according to claim 16, wherein the signal is fluorescence.

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18. The DNA array substrate according to claim 16, wherein the signal is chemical luminescence.

19. The DNA array substrate according to claim  
16, wherein the first region contains the full match  
probe and the mismatch probes having one mismatch base.  
When reacting with a normal base sequence of a nucleic  
acid.

5           20. The DNA array substrate according to claim  
16, wherein the separate regions are arranged on the  
substrate in order of total signal intensity obtainable  
by reacting with a nucleic acid having normal sequence,  
10 from a highest intensity to a lowest intensity along a  
direction of a detection.

15           21. The DNA array substrate according to claim  
16, wherein a length of the probes is 8 mer to 30 mer.

22. The DNA array substrate according to claim  
21, wherein the length of the probes is 12 mer to 25  
mer.

20           23. A system for detecting variation comprising a  
DNA array substrate according to claim 16 and a signal  
measuring apparatus which measures signals from  
separate regions of the DNA array substrate.